SOUTHWESTERN NEWS

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Researchers find local environment directly influences adult stem cell reservoirs

DALLAS – Jan. 25, 2005 – Using the common fruit fly, researchers at UT Southwestern Medical Center have discovered that an intricate set of signals released by stem cells' surroundings governs their maintenance.

These findings, available online and in today's issue of *Current Biology*, will aid stem cell researchers in understanding and potentially manipulating the delicate environments that promote adult stem cell formation, said Dr. Dennis McKearin, associate professor of molecular biology and associate dean for the Medical Scientist Training Program at UT Southwestern and senior author of the study.

"We want to understand the biochemistry behind stem cells that distinguishes them from other types of cells," Dr. McKearin said. "This work aids in understanding general stem cell biology."

The reproductive system of the female fruit fly, as in humans, contains a reservoir of adult stem cells. When the stem cells divide, they create two daughter cells, each with a distinct fate. One daughter travels away from the reservoir, divides further, and eventually becomes the egg and 'nurse' cells, which nourish the egg.

The other daughter stays near the other stem cells and is influenced by the local environment to remain a stem cell, thereby maintaining the stem cell population.

Dr. McKearin's research shows that within the local environment, or niche, of the stem cell population, stromal cells, the non-stem cells that surround and attach to stem cells, release signals that are received and processed by stem cells and the daughters remaining in the niche.

These molecular signals block certain genes from becoming active in the remaining stem cell daughters, preventing them from becoming any other kind of cell.

Genes controlling differentiation are turned off in some stem cell daughters but turned on in others, which move too far away to be influenced. Thus they develop into the egg and nurse cells.

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The success of this cell-to-cell communication is crucial. When the signals from the stromal cells are blocked, the stem cell population is gradually lost. When the signals are on all the time, or specific genes in the daughter cells are mutated, every daughter cell acts like a stem cell and the future eggs are lost.

"That stem cells are maintained by blocking gene expression suggests that the microenvironment, or niche, captures the cells and prevents them from differentiating," Dr. McKearin said. "Cells that are poised to differentiate do not, simply because of their niche."

Dr. McKearin said that in addition to their influence on stem cells, local environments or niches may influence the spread of cancer.

"Specific types of cancer often metastasize to specific other organs," he said. "For example, prostate cancer cells that respond to certain growth factors may metastasize to bone, but not liver, because they can respond to external factors in the bone niche, but not the liver niche."

The other contributor to this study is Dr. Dahua Chen, instructor in molecular biology at UT Southwestern and lead author.

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